EDITORIAL

Levodopa After Five Years

NEUROLOGISTS REMAIN ENTHUSIASTIC USERS of levodopa for the treatment of Parkinson's disease, and most begin therapy with this drug rather than with the more traditional anticholinergics. But, as pointed out by Drs. Markham, Treciokas and Diamond elsewhere in this issue of THE WESTERN JOURNAL OF MEDICINE, it is also apparent that many patients begin to slip backward after a period of a year or two of sustained improvement. Levodopa does not, therefore, cure Parkinson's disease, though many patients after five years are still less symptomatic than they were before treatment.

Why does it work at all? Dopaminergic neurons probably have inhibitory actions on other cells in the corpus striatum, many of which are interneurons that use acetylcholine as neurotransmitter. It is therefore suggested that the symptoms of parkinsonism may be due to a relative overactivity of striatal cholinergic interneurons brought about by a decrease in dopaminergic nigrostriatal inhibition and conceivably also by sprouting and reinnervation by other non-dopaminergic endings. These suggestions have by no means been firmly established. The effect of levodopa, then, is thought to be due to an increase in the ability of dopaminergic neurons that have their cell bodies in the substantia nigra to synthesize their neurotransmitter, implying that a boost in the amount of available precursor can increase neurotransmitter synthesis in diseased and possibly unaffected neurons. I do not know of any other disorder in which a deficiency in a metabolic end product can be overcome by administering a precursor and I suspect that many physicians were surprised when it turned out that levodopa did indeed work.

The dopamine level in substantia nigra can be viewed as a biochemical marker for a certain neuronal population. Reduction of dopamine in Parkinson's disease probably reflects degeneration of these cells and may be analogous to anatomical changes that occur in other systems disorders such as amyotrophic lateral sclerosis. The reason just one category of nerve cells degenerates in such diseases is a mystery which may need a future molecular biologist to unravel. This is all the more reason to applaud the pioneers who in the case of Parkinson's disease refused to accept the notion that you have to know the cause before you can find a treatment.

Application of this approach has not yet been successful in other diseases. Other disorders, such as benign essential tremor or progressive supranuclear palsy, that may be mis-diagnosed as Parkinson's disease are not helped by levodopa. It has been suggested that Huntington's chorea might be treated with an agent designed to increase GABA concentration since GABA (gamma-aminobutyric acid, another inhibitory transmitter) and the enzyme involved in its synthesis are decreased in striatum in this disease. However, it is likely that cholinergic neurons in striatum are also affected in advanced cases[2] and in an early case of Huntington's chorea there was little change in enzymes necessary for synthesis of either GABA or acetylcholine.[3]

In addition to benefiting parkinsonian patients and adding to our knowledge of the biochemistry and anatomy of the nigrostriatal system, the use of levodopa has produced side effects only rarely encountered before and not seen when levodopa is given to normal persons. Facial grimacing and restless movements of limbs are frequent toxic effects at maximum tolerated doses. Many patients prefer to keep these movements rather than reduce the dose of the drug. The off-on (or on-off) effect is not easily correlated with time of ingestion of levodopa. The not-yet-available peripherally acting dopa-decarboxylase inhibitors do not seem to help the on-off effect, though they do reduce the nausea and vomiting that many patients have. These agents appear to be much more satisfactory for this purpose than is alpha methyl dopa. It is also of interest that other effects of levodopa on growth hormone release, and on cardiac rhythm, do not appear to represent clinically significant problems.

As is also stressed by Dr. Markham and coworkers, the use of other treatments to supplement levodopa therapy should not be overlooked. Anticholinergics may still be a very useful adjunct in some patients. Amantadine is also said to be helpful, though some neurologists seem to have better

luck with it than others (I among them). Stereotaxic thalamotomy is now only rarely being done for lateralized tremor or rigidity, and the operation does not help the more bothersome problems of bradykinesia and poor balance.

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REFERENCES

1. Perry TL, Hansen J, Kloster M: Huntington's chorea—Deficiency of gamma-aminobutyric acid in brain. N Engl J Med 288: 337-342, 1973

2. McGeer PL, McGeer EG, Fibiger HC: Choline acetylase and glutamic acid decarboxylase in Huntington's chorea. Neurology 23:912-917, 1973

3. Swanson PD, Stahl WL: Biochemical abnormalities in Huntington's chorea brains. Neurology 24:370, 1974

Duty to Report Child Abuse

"MALPRACTICE LIABILITY FOR FAILING TO REPORT CHILD ABUSE" is a reprinting of an article which appeared in Volume 49, No. 2, of the *California State Bar Journal* (March-April 1974). The article represents the work and research of Richard J. Kohlman, Esq., over the past one and one-half years, and it deals with the second lawsuit in California over the past two years for a failure to report. In legalese, it is an explanation of the doctrine of negligence per se and common law medical malpractice enabling an attorney to file a suit in the civil courts on behalf of an abused child. For the physician it represents a clear warning: a failure to report suspected child abuse may mean civil liability.

While both suits have been brought in California under California law, the implication is quite strong that this type of suit would be successful in any state. The obligation of physicians to report suspected cases of child abuse, as in California, is found in the law of every state, the District of Columbia, Puerto Rico and the Virgin Islands. Coupled with this obligation is the potential civil liability for all subsequent injuries to the child when there is a failure to report suspected cases of abuse.

As a physician I would like to add that the current number of children reported for significant physical abuse in the United States is 380 per million population per year. This amounts to some 70,000 children annually. The initial mortality is 5 percent; permanent brain damage due to subdural hematoma occurs in another 5 percent. There are few diseases afflicting our children with such an incredible morbidity and mortality. Physicians, their nurses and assistants have a wonderful opportunity prenatally and postnatally and in the routine care of young children to predict, prevent and treat this devastating social and medical problem afflicting so many families.

Physicians who feel that they are doing something "against the parent" by notifying suspected cases of child abuse and aiming for early intervention to safeguard the children, should instead think of doing something "for the family." Few (less than 10 percent) of battering parents are aggressive sociopaths, paranoid schizophrenics, or plain "cruel people who torture children," although there are such persons, often impossible to treat successfully. In such cases the children have to be removed to safety and sometimes parental rights must be terminated. On the other hand, the other 90 percent of families involved respond beautifully to intensive mothering care given by sympathetic lay therapists; and they can be helped by joining Parents Anonymous, or by establishing a trusting relationship to a physician, to a public health nurse, to a social worker or any other helping person. In the great majority of cases their children can be safely returned in less than eight months after intervention begins. Clearly, therefore, the outlook is excellent and the physician's duty is unmistakable.

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Brain Abscess

THE SYMPOSIUM ON BRAIN ABSCESS presented by Drs. Yoshikawa and Goodman in this issue is an excellent review. It touches on a most appropriate set of questions. One of these is the steady mortality rate of brain abscess over the last few years. The authors make clear that there are two specific reasons for continuing high mortality. First, a brain abscess is a space occupying lesion and the mortality is more closely related to that than to the infectious aspect. Second, the lack of prompt and accurate diagnosis contributes heavily to the